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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,658	04/19/2001	Allan Bradley	S2037700210	9914

37462 7590 12/13/2006

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 12/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/839,658	**Applicant(s)** BRADLEY ET AL.	
	Examiner Teresa E. Strzelecka	**Art Unit** 1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 13 November 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *6* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *13 November 2006*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-14,17,67,68 and 70-72*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Teresa Strzelecka
12/18/06

Teresa E Strzelecka
Primary Examiner
Art Unit: 1637

Continuation of 11. does NOT place the application in condition for allowance because: Applicants' arguments were considered but were not found to be persuasive. In their arguments Applicants mostly deny that the cited references teach and suggest the claimed invention. Even though the specific teachings of each reference has been pointed out in the previously presented rejections, they are reiterated here for Applicants' convenience to illustrate the point that the cited references do teach and suggest the claimed invention.

A) Regarding the rejection of claims 1-6, 12-14, 17, 67, 68 and 72 under 35 U.S.C. 103(a) over Kallioniemi et al., McGill et al., Pollack et al., as evidenced by GibcoBRL Catalog and Mackey et al., Applicants argue that "In particular, Kallioniemi fails to disclose, teach or suggest a method that uses, in part, a plurality of immobilized nucleic acid probes that are a collection of clones that represent all of a chromosome or a genome of an organism, and contacting such probes with labeled, double-stranded genomic DNA fragments." Applicants continue to argue "Instead, Kallioniemi describes a genosensor that scans the human genome for large deletions or duplications in a single assay (emphasis added, page 14 Par. No. 0152], [0153])." Applicants follow with "In addition, Kallioniemi does not disclose, teach, or suggest a method that uses an array of clones at known locations. The Office Action asserts that FIG. 14 of Kallioniemi teaches an array of clones at known locations."

First, as recited in the previous office action, Kallioniemi et al. specifically teaches an array of nucleic acid probes which are a collection of probes cloned into a vector (page 3, 4 [0053]; page 14, [0152], [0153]). Therefore, the arrays of Kallioniemi et al. are ordered arrangments of spots with known locations, as the hybridization intensity is determined at each spot (see, for example, the description in paragraph [0152]). Therefore the genosensor of Kallioniemi et al. is made up of genomic nucleic acids cloned into vectors, and such a library spans the whole human genome (page 14, [0153]). The paragraph Applicants cite (Legend to Fig. 14), which shows the results of hybridization to a clone probe array, confirms the specific teachings of Kallioniemi with this respect. Further, It shows anticipation of step c), where the observation of each spot shows the localization of amplifications or deletions in the sample. Finally, it is clear from the description of Fig. 14 cited by Applicants that the information regarding the clones on the array is correlated with their position on the chromosome.

Therefore, Kallioniemi et al. specifically teach all of the limitations of claim 1 except the limitation that the targets which are contacted with the probes are shorter than 200 bp.

Proceeding now to the McGill et al. reference, Applicants state the following: "With reference to claim 1, McGill does not disclose, teach or suggest the particular size of the labeled, genomic nucleic acid fragments recited in claim 1. It is improper to use the probe size disclosed in McGill to render obvious a method that recites the use of a particular size of the labeled, genomic nucleic acid fragments. As recited in claim 1, these labeled, genomic nucleic acid fragments are contacted with probes."

First, to again point Applicants to the previously presented rejection, McGill et al. specifically teaches detection of chromosomal amplifications using short probes with lengths between 10 and 500 bp, with the optimal probe sequence being 20 bp long (= targets in the notation of Applicants' claim language) (col. 3, lines 56-67; col. 4, line 16; col. 5, lines 35-45 and 52-55; col. 6, lines 1-10). The statement that "it is improper to use the probe size of McGill et al. " is rather puzzling, considering that specific motivation for using such probes has been provided, both from McGill et al. and from Pollack et al.

As to the motivation to combine the references, Applicants state the following: "In addition, no evidence has been provided that the person of ordinary skill in the art would be motivated to combine Kallioniemi with the prostate cancer diagnosis methods of McGill.

Neither the Abstract of Pollack nor page 46, first paragraph of Pollack discloses, teaches or suggest the particular labeled fragment size recited in claim 1, i.e., less than about 200 bases. Thus, even if Pollack does disclose that reducing the size of genomic DNA before labeling improved labeling efficiency, without recitation of a particular size, this disclosure would not be sufficient to render claim 1 obvious."

Again the motivation to combine the references (i.e. the evidence) has been provided on page 6 of the previous office action and is recited again here for Applicants' convenience:

"Therefore, since the probes of McGill et al. are shorter than 200 bp, the result of using them in hybridization would be less probe aggregation and lower hybridization background, since each of the probes would anneal to a 20 bp sequence which appears once in 420 bp in the genome, or once every 1,099,511,627,776 bp in the genome (as compared to human genome size of 3,000,000,000 bp), that binding of such probes will be very specific, therefore reducing background and non-specific aggregation.

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used short probes of McGill et al. in the hybridization method of Kallioniemi et al. The motivation to do so, provided by McGill et al., would have been that probes with about 20 bases allows formation of duplexes which are stable and selective (col. 6, lines 1-3). Additional motivation for using short probes is provided by Pollack et al., who teach hybridization of DpnII digested and labeled genomic DNAs to cDNA arrays (Abstract; page 46, first paragraph). They found that reducing the size of genomic DNA before labeling improved labeling efficiency by providing greater accessibility of the DNA template following digestion. Such greater accessibility would also allow more specific annealing of the probes to the array."

First, the fragments generated by Pollack et al. (page 46, first paragraph) were obtained by a digest with DpnII. As one of ordinary skill knows (or would be able to find out), DpnII has a recognition site of 4 bp, therefore, it will cut on average every 256 bp in a target DNA. In reality, the range of fragments obtained would be between 200-500 bp, depending on the length of digestion. Therefore, Pollack et al., who already started with relatively short fragments, recommended making them even shorter for increased labelling efficiency. Therefore, while McGill et al. provide motivation to use short probes for increased specificity and selectivity of hebridization detection, Pollack et al. provides motivation to decrease the probe size to increase the efficiency of probe labelin, which, again, would increase hybridization sensitivity and specificity.

With regards to the Mackey et al. and Gibco BRL Catalog, the latter was used as evidence to the reference of Pollack et al. to show that Pollack et al. specifically teach labeling of both strands of genomic DNA. As to the Mackey et al. reference, it provides a motivation for labeling both strands of DNA, not a motivation to use short probes.

In conclusion, all of the limitations of claim 1 and dependent claims 2-6, 12-14, 17, 67, 68 and 70-72 are explicitely taught or suggested by the cited references, rendering the claims unpatentable.

The rejection is maintained.

B) Regarding the rejection of claims 7, 8 and 10 under 35 U.S.C. 103(a) over Kallioniemi et al., McGill et al. and Pollack et al., as evidenced by GibcoBRL Catalog, and Mackey et al., and further in view of Anderson; the rejection of claim 9 under 35 U.S.C. 103(a) over Kallioniemi et al., McGill et al. and Pollack et al., as evidenced by GibcoBRL Catalog, and Mackey et al., in view of Anderson and further in view of Waggoner et al.; the rejection of claim 11 under 35 U.S.C. 103(a) over Kallioniemi et al., McGill et al. and Pollack et al., as evidenced by GibcoBRL Catalog, and Mackey et al., in view of Anderson and further in view of Ordahl et al. and Andesron, Applicants argue that since these claims depend directly from claim 1 and the rejection of claim 1 is improper, these rejections are as well. The arguments regarding the rejection of claim 1 are presented above.

The rejections are maintained.